REMARKS

Status of the Claims

Claims 1-19 and 38-43 are pending.

Claims 1-4, 12, and 38 are amended herein.

Claims 50-56 are added as new claims.

Reconsideration is respectfully requested.

Upon entry of this Amendment and Response, claims 1-19, 38-43, and 50-56 will be pending in this application with Claims 20-37 and 44-49 having been withdrawn from further consideration by the Examiner.

New Claims

New independent Claim 50 is directed to a compound of Formula I where B is aryl or optionally substituted furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl; and R^1 is alkenyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heteroalkyl or alkylcarbonylalkyl. Thus, differences between compounds of Claim 1 and Claim 50 are (1) in claim 50, the B group may be selected from optionally-substituted aryl while in claim 1, when B is aryl it is substituted, and (2) in claim 50, the selections for R^1 do not include alkyl whereas in claim 1 they do include alkyl.

Rejection under 35 U.S.C. §112

In the Office Action of May 6, 2002, the Examiner had maintained the rejection of Claims 1-19 and 38-43 under 35 U.S.C. §112, first paragraph. In particular, that Office Action stated "...the description of prodrug...is broad and it does enable [sic] one skilled in the art to determine how the prodrug is converted to active compounds, by what mechanisms.... All these factors are uncertain ...."

The claims of the present application are directed to compounds and compositions. There is no requirement to specifically provide how a prodrug is converted to an active compound. Moreover, those skilled in the art are well aware of typical mechanisms involved in converting a prodrug to its active compound. For example, it is well known that esters, carbamates, and amides are hydrolyzed by enzymes such as hydrolases, lipases, and esterases, to generate the corresponding

hydroxides and amines, etc. However, to expedite the prosecution of this application, Claim 1 has been amended by deleting the term "prodrug" and adding the terms "an ester" and "a carbamate". Support for such amendment can be found, for example, on page 9, lines 10-19.

The May 6, 2002 Office Action also stated the variable "R" in Claim 1 should be "R_2" in the definition of A. The subscript "2" in the definition of A as being "R_2" represents the number of "R" substituents that are present on the carbon atom. Therefore, the variable "R" in Claim 1 in the definition of A is correct.

As suggested by the Office Action of May 6, 2002, variables X and Y have been amended to CH in view of the restriction requirement. In particular, Formula I has been redrawn by deleting variables X and Y and replacing them with CH groups. In addition, in view of the new structure for Formula I, Claims 2 and 38 have been amended to delete the variables X and Y.

It is gratefully acknowledged that in the Advisory Action of September 6, 2002, it was found that the foregoing amendments and remarks were sufficient to overcome the Section 112 rejections set forth in the Office Action of May 6, 2002.

Rejection under 35 U.S.C. §102

In the Office Action of May 6, 2002, a number of rejections were set forth under 35 U.S.C. §102(b) as allegedly being anticipated by the cited references. It is well established that claims are anticipated if, and only if, each and every element as set forth in the claim is found in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051 (Fed. Cir. 1989). As discussed in detail below, none of the cited references discloses every element of the present invention.

The Barton Reference

In the Office Action of May 6, 2002, the Examiner had maintained rejection of Claims 1-5 under 35 U.S.C. §102(b) as allegedly being anticipated by Barton et al. (J. Am. Chem. Soc. 1993). In particular, the Office Action states that the term alkyl "should be given the broadest interpretation that includes fluorine substituted alkyl."

The term "alkyl" is defined on page 3, lines 17-19, as being "a linear saturated monovalent hydrocarbon radical of one to six carbon atoms or a branched saturated monovalent hydrocarbon radical of three to six carbon atoms...." (emphasis added). Moreover, the standard definition for

alkyl in the art is having a generic formula C_nH_{2n+1}. (See exhibit A, page 34 of *Hawley's Condensed Chemical Dictionary*, 13th Ed., Lewis, Sr., John Wiley & Sons, Inc., New York, NY, 1997). Furthermore, halogen substituted alkyl groups are separately defined in the present application as "haloalkyl." (See page 5, lines 7-9.)

Therefore, the definition of "alkyl" does not include a trifluoromethyl group. Accordingly, the 35 U.S.C. §102(b) rejection of the claims based on Barton should be withdrawn.

The Okada Reference

In the Office Action of May 6, 2002, claims 1-5 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by the Okada reference ("Okada").

The compounds discussed in Okada are different from the compounds claimed herein. For example, the variable R^1 of Formula I of the present invention is limited to alkyl, alkenyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heteroalkyl, and alkylcarbonylalkyl. As defined on page 6, lines 9-11, the term "heteroaralkyl" refers to a radical $-R^aR^b$ where R^a is an alkylene group and R^b is a heteroaryl group. Thus, when R^1 includes a pyrimidine ring (a heteroaryl group), it is attached to the nitrogen atom by an alkylene linker.

In contrast, if the pyrimidine ring of the compound discussed in Okada corresponds to R^1, the Okada compound has the pyrimidine ring attached directly to the nitrogen atom, i.e., without an alkylene linker. Thus, Okada discloses a different compound from the compounds of the present invention. Accordingly, the 35 U.S.C. §102(b) rejection based on Okada should be withdrawn.

The Billman Reference

In the Office Action of May 6, 2002, claims 1-5 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Billman et al. (J. Org. Chem., 1962) (hereinafter "Billman").

Compound V of Billman that is referred to in that Office Action has an amino moiety that is substituted with an ethyl group and a benzyl group, which corresponds to groups R^1 and –A–B, respectively, of Formula I of the present invention. Specifically, the phenyl ring of the benzyl group of Compound V in Billman may correspond to the variable "B" of Formula I of the present invention.

As amended, the moiety B is defined in claim 1 as substituted aryl or optionally substituted furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl. Thus, the aryl group is a

substituted aryl group. In contrast, the phenyl group of Compound V in Billman is unsubstituted. Accordingly, the 35 U.S.C. §102(b) rejection based on the Billman should be withdrawn.

As for new claims 50-56, the nitrogen atom in Compound V of Billman comprises an ethyl group (i.e., an alkyl group). New Claim 50 does not include alkyl as a selection for R^1 .

The Katritzky Reference

In the Office Action of May 6, 2002, claims 1-5 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Katritzky et al. (Synthetic Communications, 1993) (hereinafter "Katritzky").

Compound 5 of Katritzky that is referred to in that Office Action has an amino moiety that is substituted with a butyl group and a 3-phenylpropyl group, which corresponds to groups R^1 and –A–B, respectively, of Formula I of the present invention. Specifically, the phenyl ring of the 3-phenylpropyl group of Compound 5 in Katritzky corresponds to the variable "B" of Formula I of the present invention. Similar to Compound V of Billman, the phenyl ring of Compound 5 of Katritzky is unsubstituted.

As stated above in the discussion regarding Billman, the aryl group of the variable "B" of the present invention as defined in claims 1-5 is a substituted aryl group. Therefore, the 35 U.S.C. §102(b) rejection based on Katritzky should be withdrawn.

As for new claims 50-56, the nitrogen atom in Compound 5 of Katritzky comprises a butyl group (i.e., an alkyl group). New Claim 50 does not include alkyl as a selection for R^1 .

It is gratefully acknowledged that in the Advisory Action of September 6, 2002, it was found that the foregoing amendments and remarks were sufficient to overcome the Section 102 rejections set forth in the Office Action of May 6, 2002, i.e., based on Barton, Okada, Billman, and Katritzky.

Rejection under 35 U.S.C. §103

In the Office Action of May 6, 2002, claims 1-5, 12, and 13 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Dinsmore et al. (Bioorganic and Medicinal Chemistry, 1999) (hereinafter "Dinsmore"). The Office Action of May 6, 2002, states Compound 8a of Dinsmore differs from the compounds of the present invention "only in the nature of the substituent on the nitrogen atom (R is H in reference and R1 is alkyl in the instant invention)." The Office

Action then stated "the reference teaches the equivalence of H and alkyl in the definition of R.... Thus, one of ordinary skill in the art would have been motivated *to select* the claimed compounds *from the genus in the reference* since such compounds would have been suggested by the reference as a whole" (emphasis supplied herein).

However, the compounds discussed in Dinsmore are structurally different from the compounds of the present invention. The imidazolyl moiety of Compound 8a of Dinsmore is substituted with a 4-cyanobenzyl group. In contrast, in the instant case, the definition of heteroaryl on page 5, line 21, to page 6, line 8, does not include a substituted benzyl moeity. There was a typographical error in the specification as filed in that a "closed parentheses" [i.e., ") "] was missing following the word "phenylalkyl" at page 5, line 28. This typographical error is corrected herein. This is an obvious typographical error such that its correction is not new matter [*see*, MPEP 2163.07(a) ("An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction")].

More specifically, it is obvious that there had intended to be a closed parentheses in the specification as filed following "phenylalkyl" at page 5, line 28, considering that: 1) there is an open parentheses [i.e., " ("] on page 5, line 27, following –COR, which needs to be partnered with a closed parentheses, with the only possible or grammatically-acceptable location being after "phenylalkyl" on line 28; 2) the definition of substituents for aryl groups (at page 4), includes the same reference to –COR (at page 4, lines 11-12) with the closed parentheses following "phenylalkyl"; and 3) the definition of substituents for heterocycyl groups (at page 6), also includes the same reference to –COR (at page 6, lines 20-21), with a closed parentheses following "phenylalkyl."

Accordingly, the optional substituents for heteroaryl do not include a benzyl group directly attached to the heteroaryl ring. Rather, the benzyl group may be attached to the heteroaryl via a linker which is –CO-, -$(CR'R'')_n$-COO-, or–$(CR'R'')_n$-$CONR^a$-. Thus, there is no overlap between compounds of the present invention and those disclosed in Dinsmore, and the instantly-claimed compounds cannot be selected from any alleged genus based on Dinsmore. Additionally, the compounds do not share a common utility as the Dinsmore compounds are FTase inhibitors, and the instantly-claimed compounds are COX-2 inhibitors. Thus, there is no basis to find an expectation

of similar properties. There is no basis for an obviousness rejection based on alleged, close structural similarity (see, MPEP 2144.09).

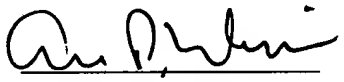
Accordingly, the 35 U.S.C. §103(a) rejection based on Dinsmore should be withdrawn.

CONCLUSION

For the Examiner's convenience, Applicant has attached as Appendix A, a listing of the claims as they will read following entry of the instant amendments.

It is believed the case is now in condition for allowance. If the Examiner believes that a telephone conference would expedite the prosecution of this application, applicant respectfully requests that the Examiner telephone the undersigned at (650) 852-1141.

Respectfully submitted,



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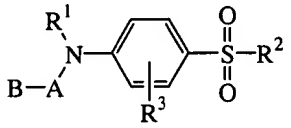
APPENDIX B
Pending Claims 1-19, 38-43, and 50-56

1. (Amended Herein) A compound of the formula (I):



Formula I

wherein:

A is $-(CR_2)_n-$ where *n* is 1, 2 or 3 and each R is independently hydrogen or alkyl;

B is substituted aryl, or optionally substituted heteroaryl, wherein said heteroaryl is furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl;

R^1 is alkyl, alkenyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heteroalkyl or alkylcarbonylalkyl;

R^2 is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, or $NR^{13}R^{14}$ wherein:

R^{13} is hydrogen or alkyl;

R^{14} is hydrogen, alkyl, alkenyl, acyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aralkyl, hydroxyalkyl, alkoxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, or aminoalkyl;

R^3 is hydrogen, alkyl, halo, nitro, cyano, hydroxy, alkoxy; or an ester, a carbamate, or a pharmaceutically acceptable salt thereof.

2. (Amended Herein) The compound of Claim 1, wherein R^3 is hydrogen.

3. (Amended Herein) The compound of Claim 2 wherein B is substituted aryl.

4. (Amended Herein) The compound of Claim 3 wherein B is substituted phenyl.

5. (original). The compound of Claim 4 wherein R^1 is alkyl, cycloalkyl, cycloalkyl-alkyl, heterocyclyl, heterocyclylalkyl or heteroalkyl.

6. (original). The compound of Claim 5 wherein R^1 is heteroalkyl.

7. (original). The compound of Claim 6 wherein R^1 is alkylsulfonylalkyl.

8. (original). The compound of Claim 7 wherein R^2 is alkyl.

9. (original). The compound of Claim 8 wherein A is $-(CH_2)-$.

10. (original). The compound of Claim 7 wherein R^2 is $NR^{13}R^{14}$ wherein R^{13} and R^{14} are hydrogen.

11. (original). The compound of Claim 10 wherein A is $-(CH_2)-$.

12. (Amended Herein) The compound of Claim 2 wherein B is optionally substituted heteroaryl, wherein heteroaryl is furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl.

13. (original). The compound of Claim 12 wherein R^1 is alkyl, cycloalkyl, cycloalkyl-alkyl, heterocyclyl, heterocyclylalkyl or heteroalkyl.

14. (original). The compound of Claim 13 wherein R^1 is heteroalkyl.

15. (original). The compound of Claim 14 wherein R^1 alkylsulfonylalkyl.

16. (original). The compound of Claim 15 wherein R^2 is alkyl.

17. (original). The compound of Claim 16 wherein A is $-(CH_2)-$.

18. (original). The compound of Claim 15 wherein R^2 is $NR^{13}R^{14}$ wherein R^{13} and R^{14} are hydrogen.

19. (original). The compound of Claim 18 wherein A is $-(CH_2)-$.

38. (Amended Herein) The compound of Claim 1 wherein:
R^1 is heteroalkyl, wherein the heteroalkyl is alkylsulfonylalkyl; and
B is substituted aryl.

39. (original). The compound of Claim 38, wherein R^2 is alkyl.

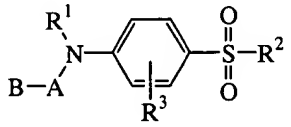
40. (original). The compound of Claim 39, wherein A is $-(CH_2)-$.

41. (original). The compound of Claim 38, wherein R^2 is NH_2.

42. (original). The compound of Claim 41, wherein A is $-(CH_2)-$.

43. (original). A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 and a pharmaceutically acceptable excipient.

50. (New) A compound of the formula:



wherein:

A is $-(CR_2)_n-$ where n is 1, 2 or 3 and each R is independently hydrogen or alkyl;
B is aryl or optionally substituted heteroaryl, wherein said heteroaryl is furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl;
R^1 is alkenyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heteroalkyl or alkylcarbonylalkyl;
R^2 is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, or $NR^{13}R^{14}$ wherein:
R^{13} is hydrogen or alkyl;

R^{14} is hydrogen, alkyl, alkenyl, acyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aralkyl, hydroxyalkyl, alkoxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, or aminoalkyl;

R^3 is hydrogen, alkyl, halo, nitro, cyano, hydroxy, or alkoxy; or

an ester, a carbamate, or a pharmaceutically acceptable salt thereof.

51. (New) The compound of Claim 50, wherein R^1 is heteroalkyl.

52. (New) The compound of Claim 51, wherein R^1 is alkylsulfonylalkyl.

53. (New) The compound of Claim 52, wherein R^2 is alkyl.

54. (New) The compound of Claim 53, wherein A is $-(CH_2)-$.

55. (New) The compound of Claim 52, wherein R^2 is $NR^{13}R^{14}$ wherein R^{13} and R^{14} are hydrogen.

56. (New) The compound of Claim 55, wherein A is $-(CH_2)-$.

* * * * * *